In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-926V

(to be published)

MARTIN MCGRAIL *as father and natural guardian of minor* S.M., *and* AMY MCGRAIL *as mother and natural guardian of minor* S.M.,	*	Chief Special Master Corcoran
Petitioners,	*	Filed: March 23, 2021
v.	*	Ruling on Entitlement; Transverse Myelitis; Hepatitis B Vaccine; Molecular Mimicry; *Althen* Prong One; *Althen* Prong Three; Treater Support
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Jeffrey S. Pop, Esq., Jeffrey S. Pop & Assoc., Beverly Hills, CA, for Petitioners.

Christine Becer, U.S. Department of Justice, Washington, DC, for Respondent.

RULING ON ENTITLEMENT[1]

On July 10, 2017, Martin and Amy McGrail, as parents and natural guardians of S.M., a minor, filed this action seeking compensation under the National Vaccine Injury Compensation Program (the "Program"). ECF No. 1. The Petitioners allege that a Hepatitis B vaccine administered to S.M. on July 14, 2014, caused her to incur transverse myelitis ("TM"). Although an initial hearing in the matter was held in late-January 2020, the parties have since jointly agreed

[1] This Ruling will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published Ruling's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire Ruling will be available to the public in its current form. *Id.*

that the matter could be resolved via ruling on the record, rather than by holding a follow-up hearing for testimony from the remaining experts and other additional fact witnesses.

Having reviewed the record, all expert reports and associated literature, and listened to those witnesses and experts who testified at the 2020 hearing, I hereby find that Petitioners are entitled to a damages award. Petitioners have preponderantly established that S.M. likely experienced TM post-vaccination, rather than acute flaccid myelitis ("AFM") as Respondent maintains. Petitioners have also met their burden under *Althen v. Sec'y of Health & Hum. Servs.,* 418 F.3d 1274, 1278 (Fed. Cir. 2005)—although resolution of this case presents a very close call, since Petitioner's overall showing on the first and third *Althen* prongs was not notably robust when evaluated closely.

I. Fact History

S.M. was born on October 1, 2013, via spontaneous vaginal delivery without complication. Ex. 18 (filed on compact disk) at 65; Affidavit of Amy McGrail, filed as Ex. 1 (on compact disk) at 1 ("Affidavit"). Prior to her receipt of the vaccine at issue, S.M. was a healthy child without any significant medical conditions. S.M. did suffer from seasonal allergies for which she received nebulizer treatments with Xopenex and Pulmicort as needed. Ex. 7 (filed on compact disc) at 105. S.M.'s family history does not include any serious medical conditions relevant to the claim. Ex. 7 at 94–95; Affidavit at 1.

On June 20, 2014 (a few weeks before receiving the vaccine at issue), S.M. was seen by Dr. Mary Yee, one of S.M.'s pediatricians, for a three-day history of congestion, cough, and yellow nasal discharge. Ex. 7 at 104. S.M. was deemed afebrile, however, with a rectal temperature of 99 degrees. *Id.*; Tr. at 89. She was prescribed antibiotic treatment with amoxicillin, and her symptoms dissipated by July 8, 2014. Tr. at 137, 158.

The following month, on July 14, 2014, Ms. McGrail took S.M. to Pediatric Associates in Neptune, New Jersey for a routine well-child visit and to receive the third dose of the Hepatitis B vaccine. Ex. 7 at 94. No medical concerns were raised during the visit, and Dr. Yee noted that S.M. did not experience any immediate reaction to the vaccination. *Id.*

Three days later, at approximately 3:30 p.m. on July 17, 2014, Ms. McGrail received a phone call from S.M.'s daycare informing her that S.M. was sleepy, irritable, and had developed a fever and therefore needed to be picked up. Affidavit at 2; Ex. 5 (filed on compact disk) at 23–31. After retrieving S.M., Ms. McGrail took her to Dr. Yee to be evaluated for a newly developed fever, limpness, and difficulty breathing. Affidavit at 2. Dr. Yee noted that S.M. had a fever of 100.6 degrees, was lethargic, and was constantly crying in pain. Ex. 7 at 102. Dr. Yee recommended S.M. be taken to the emergency department for further evaluation. *Id.*; *see also* Ex. 9 (filed on compact disk) at 29–30.

Upon arriving at Jersey Shore University Medical Center, S.M. was evaluated in the emergency department at approximately 5:20 p.m. by Dr. Richard Sultan, D.O. Ex. 5 at 19–21, 24. A physical examination conducted by Dr. Sultan revealed that S.M. had a fever and was in acute neurological distress. *Id.* at 20–21. He noted that S.M. had good motor control of her head but had no control of her trunk, was having difficulty breathing, and was exhibiting spontaneous movement of her extremities. *Id.* Based upon these observations, Dr. Sultan's differential diagnoses included acute disseminated encephalomyelitis, TM, botulism, Guillain-Barré syndrome ("GBS"), tick paralysis, and myasthenia gravis. *Id.* at 21. To further refine his diagnosis, Dr. Sultan ordered several diagnostic tests, including an MRI and cerebral spinal fluid ("CSF") test. *Id.* S.M. was admitted to the pediatric intensive care unit at 5:28 p.m. and broad-spectrum antibiotics were administered. *Id.* at 31, 38; Ex. 105 filed Oct. 15, 2019 (ECF No. 35-9) at 412.

At around 6:30 p.m. on July 17th, S.M. underwent a lumbar puncture to collect a CSF specimen. Ex. 4 (filed on compact disk) at 64. Analysis of the sample revealed elevated protein levels. *Id.* A few hours later, at 11:58 p.m., S.M. underwent a spinal MRI. Ex. 5 at 85. The results of that MRI showed "[d]iffuse increased signal intensity within the cervical cord and upper thoracic cord…with expansion of the cord particularly within the cervical spine without evidence of enhancement following the administration of contrast." *Id.* These findings were consistent with Dr. Sultan's initial TM diagnosis, and he thereafter began a five-day course of treatment with Solumedrol.[2] *Id.*; Ex. 105 at 413. Within two days of this treatment, S.M. experienced improved mobility of her lower extremities, though her upper extremities remained flaccid. Ex. 5 at 108. A repeat MRI conducted on July 23, 2014 showed "significant improvement of edema within the cervical cord" with the lesion now extending only between C3 and T4 where it had previously extended from C2 to T6. *Id.* at 88.

In the course of S.M.'s initial treatment, consideration was given to whether an infectious cause could be identified for her neurologic presentation. Thus, on July 19, 2014, S.M. was evaluated by Dr. Aswine Bal, an infectious disease specialist. Ex. 5 at 17–18. His physical examination of S.M. revealed hypotonia in her upper extremities and decreased tone in her lower extremities. *Id.* at 17. Though Dr. Bal observed some movement and brisk reflexes in S.M.'s lower extremities, he noted that she was still unable to move her arms or sit unassisted. *Id.* Regarding the proposed diagnosis of TM, Dr. Bal agreed that the MRI results of July 17th supported the diagnosis, and explained that TM is usually preceded by a viral infection or vaccination. *Id.* at 18. An extensive infectious disease work-up was positive for a rhinovirus infection, so broad-spectrum antibiotic treatments were discontinued. Ex. 100, filed Oct. 15, 2019 (ECF No. 35-3) at 65; Ex. 105 at 419, 484.

S.M. was discharged from Jersey Shore University Medical Center on July 31, 2014, with a diagnosis of TM. Ex. 5 at 103. She was transferred to the Children's Hospital of Philadelphia

[2] Solumedrol is an anti-inflammatory synthetic glucocorticoid. *Dorland's Medical Dictionary Online*, https://www.dorlandsonline.com/dorland/definition?id=89219 (last visited Mar. 3, 2021).

("CHOP") for additional treatment. *Id.* Upon her admission to CHOP, S.M. was noted to have persistent hypotonia and absent reflexes in her upper extremities, but she was able to spontaneously move and had brisk reflexes in her lower extremities. Ex. 100 at 67. S.M. continued to exhibit breathing difficulty leading treaters to intubate her. *Id.* at 71–72. Because S.M. continued to experience intermittent fevers, additional laboratory studies were ordered. *Id.* at 71.

On August 1, 2014, S.M.'s cultures again revealed the presence of a rhinovirus infection, with no other infections detected. Ex. 7 at 430–31. Based on these results, in addition to the MRI and CSF studies that were conducted at Jersey Shore University Medical Center, treaters at CHOP initially suspected that S.M. was "suffering from a monophasic demyelinating event rather than the first presentation of a chronic demyelinating disorder." Ex. 100 at 81. Thus, an eight-day course of Plasmapheresis[3] ("PLEX") treatment was initiated. *Id.* at 81–82, 184. On August 12, 2014, S.M. underwent a repeat MRI which showed residual non-enhancing abnormalities from C3 to T2 with "subtle signal abnormality in the cord at the T10 level." *Id.* at 174–75.

S.M. received her final PLEX treatment on August 13, 2014, and was evaluated for discharge to a rehabilitation facility on August 14, 2014. Ex. 100 at 183. During her physical evaluation, S.M. was noted to have "4/5 strength" and normal responses to touch in both legs, but 0/5 strength in her upper extremities—though she was now exhibiting some spontaneous movement in her right wrist and left fingers. *Id.* at 184. She also appeared to have regained some muscle tone in both her upper and lower extremities. *Id.* S.M. was thereafter discharged to Children's Specialized Hospital for inpatient rehabilitation with Dr. Michele Fantasia. *Id.* at 186; *see generally* Ex. 6 (filed on compact disk). After completing intensive physical and occupational therapy, S.M. showed continued improvement in her physical condition, but she did not return to her pre-vaccination baseline. Ex. 6 at 93–99. She was discharged from Children's Specialized Hospital on September 14, 2014.

Since September 2014, S.M. has continued to pursue outpatient physical and occupational therapy with noted improvement. Ex. 6 at 93–99, 876–78, 892–94, 904–06, 918–20, 954–56; Ex. 14 (filed on compact disk) at 1–7. On January 5, 2017, S.M. was re-evaluated by CHOP neurologist, Dr. Amy Waldman. Ex. 14 at 1–7. During her evaluation, Dr. Waldman noted that S.M. had not experienced any worsening or new episodes of neurologic dysfunction since the initial onset of her symptoms in July 2014. *Id.* at 1. Regarding S.M.'s diagnosis, Dr. Waldman acknowledged the original TM diagnosis S.M. had received during her initial hospital admission, but she also considered the possibility that S.M. had suffered from AFM—a condition that became prevalent in the fall of 2014 and is thought to be associated with Enterovirus D68 infections. *Id.* at 5.

[3] Plasmapheresis is a procedure in which plasma is removed from the blood and is then transfused back into the body with added donor components such as frozen plasma or albumin. *Dorland's Medical Dictionary Online*, https://www.dorlandsonline.com/dorland/definition?id=39455&searchterm=plasmapheresis (last visited Mar. 3, 2021).

To date, S.M. "remains profoundly quadriplegic" with moderate to severe spasticity. Tr. at 123. Her quadriplegia makes her more susceptible to other conditions including orthopedic problems, scoliosis, bladder complications, urinary tract infections, kidney disease, bowel dysfunction, megacolon and perforation, and skin breakdown. *Id.* at 124, 164. S.M.'s condition is not expected to improve. *Id.* at 124, 140.

II. Experts and Testifying Witnesses

A. *Petitioners' Fact Witnesses and Treaters*

1. Mr. Martin McGrail

Mr. McGrail, S.M.'s father, offered testimony at the entitlement hearing.[4] *See generally* Tr. at 132–47. He began by discussing S.M.'s health prior to receiving the third dose of the Hepatitis B vaccine, noting that she was an overall healthy child who only occasionally required allergy medications (Pulmicort and Xopenex). *Id.* at 134–35, 137. Mr. McGrail did not recall S.M. experiencing any unusual health problems close in time to her vaccination. *Id.* at 137. He did note that approximately three or four weeks before her vaccination, S.M. experienced some congestion and was diagnosed with an upper respiratory infection, but it was treated with antibiotics and had completely resolved by the time she received the vaccine. *Id.* at 142–43.

According to Mr. McGrail, Ms. McGrail took S.M. to her doctor's appointment on the morning of July 14, 2014. Tr. at 137–38. Three days later, on July 17, 2014, Mr. McGrail recalls that S.M. appeared healthy and was not exhibiting any signs of illness (fever, cough, runny nose, etc.). *Id.* at 138. He did, however, recall that S.M. was given a nebulizer treatment with Pulmicort for a cough and shortness of breath—symptoms the McGrails attributed to S.M.'s allergies. *Id.* at 143–44; Ex. 5 at 32. S.M. was also given Tylenol for teething discomfort at that time. Tr. at 143–44; Ex. 5 at 32. That afternoon, he received a phone call from Ms. McGrail informing him that she had to pick S.M. up from daycare to take her to the pediatrician. Tr. at 139. Mr. McGrail later learned that S.M. was taken to the emergency room, and he arrived at the hospital that evening. *Id.* at 139. At the hospital, Dr. Sultan informed Mr. McGrail of S.M.'s TM diagnosis and that her condition could be associated with a viral illness or vaccination. *Id.* at 139, 146–47.

2. Ms. Amy McGrail

Ms. McGrail offered both a written affidavit and testimony during the entitlement hearing. Tr. at 149–69. She described S.M. as an overall healthy baby prior to receiving the third dose of

[4] As noted above, an initial hearing was held in January 2020, at which time a number of fact witnesses and experts testified. But not all experts were heard at this time; in particular, Respondent's experts did not testify.

the Hepatitis B vaccine. *Id.* at 152–54. While S.M. did suffer from a milk protein allergy in addition to seasonal allergies, those conditions were well managed with special formula and allergy medications. *Id.*

Ms. McGrail recalled taking S.M. to her pediatrician, Dr. Yee, on the morning of July 14, 2014 for a routine visit and vaccination. Tr. at 153, 159. According to her, S.M. was in good health on the day of her appointment. *Id.* at 159–60. When S.M. awoke on the morning of July 17, 2014, Ms. McGrail did not observe any unusual signs or symptoms of illness before taking S.M. to daycare. *Id.* at 160–61. Though she did not recall administering Xopenex and Pulmicort to S.M. that morning, she indicated that giving S.M. these medications was not unusual given the frequency of S.M.'s allergy symptoms. *Id.* at 161–62, 166–67.

At approximately 3:00 p.m. that day, Ms. McGrail received a phone call from S.M.'s daycare informing her that S.M. had developed a fever and needed to be picked up earlier than usual. Tr. at 162. On the way to pick up S.M., Ms. McGrail scheduled an emergency appointment with Dr. Yee to have S.M. evaluated for her fever. *Id.* Following an examination of S.M., Dr. Yee urged Ms. McGrail to take S.M. to the emergency room for further evaluation. *Id.* at 163. A few hours after S.M.'s admission to the Jersey Shore University Medical Center, Ms. McGrail was told that S.M. was suffering from TM and required steroid treatment. *Id.* She did not recall ever being told that S.M. had a viral infection while at Jersey Shore University Medical Center. *Id.* at 164. According to Ms. McGrail, S.M. was eventually transferred to CHOP for PLEX treatments, and it is at that time when she first became aware that S.M. was concurrently experiencing a rhinovirus infection. Tr. at 164.

3. Dr. Mary Yee

Dr. Yee, S.M.'s pediatrician of approximately six years, provided testimony at the entitlement hearing on Petitioners' behalf. Tr. at 62–109. Dr. Yee completed her medical education at SCB Medical College in India before completing her residency training in Cleveland, Ohio. *Id.* at 63. She is a board-certified pediatrician and has been working as a primary care physician for approximately twenty-eight years. *Id.*

As Dr. Yee recalled, S.M. was in overall good health and was developing normally prior to receiving the third dose of the Hepatitis B vaccine. Tr. at 68–94. Any health concerns for which S.M. was seen for, including an E. coli infection, bronchitis, bronchiolitis, colic, and allergies, are common among children, and S.M. responded well to the treatments she received for these various issues. *Id.* at 70–71, 76–79, 82–87, 89–91. On the morning of July 14, 2014, Dr. Yee recalled that S.M. appeared healthy and developmentally normal. *Id.* at 91–93. She administered the third dose of the Hepatitis B vaccine and did not note any immediate adverse reactions. *Id.*

When S.M. returned to Dr. Yee in the afternoon of July 17, 2014, S.M. seemed very irritable and lacked muscle tone. Tr. at 95. Dr. Yee performed an extensive physical evaluation, but her examination did not reveal any signs of illness. *Id.* at 96. Based upon her observations, Dr. Yee recommended S.M. be taken to the emergency department to be evaluated by a neurologist. *Id.* at 95.

Since S.M. first received her TM diagnosis, Dr. Yee has continued to see S.M. for primary care visits. Tr. at 97; Ex. 140 at 21–109. Dr. Yee described S.M.'s present condition as "not good"—she is paraplegic and continues to exhibit poor muscle tone and spasticity. Tr. at 99. She is unable to urinate on her own and thus requires catheterization. *Id.* at 97. According to Dr. Yee, S.M. continues to need extensive physical and occupational therapy for her condition. *Id.* at 99.

4. Dr. Michele Fantasia, M.D.

Dr. Fantasia provided a single report and testimony at the entitlement hearing on behalf of Petitioners. *See* Dr. Fantasia Report, filed as Ex. 83 on June 17, 2019 (ECF No. 33-2) ("Fantasia Rep."); Tr. at 110–31.

Dr. Fantasia is a board-certified pediatric physiatrist specializing in physical medicine and rehabilitation. Tr. at 110. She received her bachelor's degree (biology) from Fairleigh Dickinson University, followed by her medical degree from the New Jersey Medical School. Dr. Fantasia Curriculum Vitae, filed as Ex. 84 on June 17, 2019 (ECF No. 33-3) ("Fantasia CV"); Tr. at 111. She then completed her internship and residency in pediatrics, physical medicine, and rehabilitation at the University of Medicine and Dentistry of New Jersey before obtaining board certification in these subjects. Fantasia CV at 1; Tr. at 111–12. Currently, Dr. Fantasia serves as the Director of the Spinal Cord Injury and General Rehabilitation programs at Children's Specialized Hospital in New Brunswick, New Jersey. Fantasia CV at 1; Tr. at 112. Dr. Fantasia first became familiar with S.M.'s case in August 2014, when S.M. was admitted to Children's Specialized Hospital for inpatient rehabilitation. Tr. at 113. She served as S.M.'s treating physiatrist during S.M.'s admission, and she has continued to follow-up with S.M. since that time. *Id.*

In her testimony, Dr. Fantasia discussed the defining characteristics of both TM and AFM. Tr. at 113–16. She described TM as an "autoimmune disease of the spinal cord with still debated unclear etiologies" that results in spastic paralysis. *Id.* at 113. She also emphasized that TM is a disease that targets both gray and white matter of the spinal cord. *Id.* at 115. This characteristic, according to Dr. Fantasia, is what primarily distinguishes TM from AFM—a disease that is generally limited to gray matter of the anterior horn cells of the spinal cord. *Id.* at 114–15.

Another distinguishing feature highlighted by Dr. Fantasia between TM and AFM was the spastic nature of TM-induced paralysis, as compared to the flaccid paralysis caused by AFM. Tr. at 113–14, 116, 118–19, 127. CSF studies can also help differentiate between a TM and AFM diagnosis, because protein levels are typically higher in cases of TM. *Id.* at 115, 131. Dr. Fantasia did acknowledge, however, that distinguishing between TM and AFM can be difficult during the acute phase because the initial "findings can be very similar." *Id.* at 115, 127. Over the course of her twenty-year-long career, Dr. Fantasia has seen approximately sixty patients suffering from TM, but only about three or four patients with AFM. *Id.* at 114–15. She attributed this disparity to the fact that AFM—which is a subtype of acute flaccid paralysis—was not defined until 2014, and was therefore not a diagnosis that physicians would have considered. *Id.* at 115, 128.

Based upon the medical records made available to her, plus her direct experience treating S.M., Dr. Fantasia opined that S.M. more likely than not suffered from TM. Tr. at 114, 117, 130. Though she largely deferred to the opinions of the neuroradiologist who interpreted S.M.'s MRI studies, Dr. Fantasia offered additional evidence based on her own observations of S.M.'s condition to support her conclusion. *Id.* at 114, 118–20. She began by noting that S.M. exhibits spastic paralysis, hypertonia[5], increased reflexes, and clonus[6]. *Id.* at 119. These symptoms are caused by damage to both motor and sensory neurons, and are typical of TM. *Id.* By contrast, if S.M. had experienced AFM, her muscle tone would have remained flaccid or "floppy." *Id.* at 119, 127. She also noted that S.M. suffers from severe sensory deficits, leaving her more prone to tissue damage. *Id.* at 122. While some sensory deficits may be observed in AFM cases, they tend to be less profound than those seen in TM. *Id.* The severity and extent of S.M.'s sensory and motor deficits led Dr. Fantasia to conclude that the TM diagnosis she had received was likely accurate. *Id.* at 114, 130.

5. Dr. Aswine Bal, M.D., MPH

Though Dr. Bal, an infectious disease specialist, did not testify at the entitlement hearing, he offered a report in support of Petitioners' claim. *See* Report, filed as Ex. 108 on Jan. 16, 2020 (ECF No. 44-1) ("Bal Rep."). In it, Dr. Bal outlined his involvement in the treatment of S.M., including the clinical findings he considered in rendering his TM diagnosis. *Id.*

Dr. Bal completed his undergraduate education at Ravenshaw University in Cuttak, India. Bal Curriculum Vitae, filed as Ex. 109 on Jan. 16, 2020 (ECF No. 44-2). He then obtained his Bachelor of Medicine and Bachelor of Surgery from S.C.B. Medical College in Cuttak, India

[5] Hypertonia describes excessive tone of the skeletal muscles, so that they have increased resistance to passive stretching and reflexes are often exaggerated; this usually indicates upper motor neuron injury. Dorland's Illustrated Medical Dictionary 886 (33rd ed. 2020) (hereinafter "Dorland's").

[6] Clonus describes a continuous rhythmic reflex tremor initiated by the spinal cord below an area of spinal cord injury, set in motion by reflex testing. Dorland's at 368.

before completing a rotating internship at S.C.B. Medical College Hospital. *Id.* at 1. Dr. Bal went on to receive a master's degree in public health from Yale University while simultaneously completing a residency in preventative medicine at the Yale University School of Medicine. *Id.* He then completed a residency in pediatrics at Newark Beth Israel Medical Center in Newark, New Jersey before returning to Yale University to complete a fellowship in pediatric infectious disease. *Id.* Currently, Dr. Bal serves as a professor of pediatrics at Rutgers Robert Wood Johnson Medical School, in addition to his clinical practice as an attending physician in pediatric infectious disease at Jersey Shore University Medical Center. *Id.* at 2.

Dr. Bal's report notes that he first became involved in S.M.'s treatment on July 19, 2014—hence contemporaneous with her vaccination and immediate hospitalization days thereafter. Bal Rep. at 1. At that time, S.M. had already undergone an MRI and CSF studies, and her treating neurologist, Dr. Sultan, had already proposed a working diagnosis of TM. *Id.* at 1–2. During his initial infectious disease consultation with S.M., Dr. Bal recommended she undergo viral studies, including a viral respiratory panel. *Id.* at 2. He was, however, unable to find the reported laboratory results for those tests despite diligent efforts to locate them.[7] *Id.* Dr. Bal was thus unable to explain the report of a positive rhinovirus test in the July 30, 2014 transfer note, but nonetheless concluded that even *if* S.M. was at the time suffering from a rhinovirus infection, it was unlikely to have contributed to her developing TM. *Id.* He did not, however, provide an explanation or references in support of this opinion.

After eliminating infectious etiologies for S.M.'s condition, Dr. Bal considered the possibility that the Hepatitis B vaccination S.M. had received just a few days prior to the onset of her symptoms may have played a causal role. Bal Rep. at 2–3. He found several case reports describing instances of TM and other demyelinating conditions post-vaccination, though he also acknowledged that case reports are insufficient to establish a causal association. *Id.* at 3. Thus, Dr. Bal concluded that S.M.'s Hepatitis B vaccine could at least not be ruled out as the cause of S.M.'s condition. *Id.*

B. *Petitioners' Experts*

1. Dr. Jeffrey Silverman, M.D.

Dr. Silverman, a radiologist, provided one expert report and testified at the entitlement hearing on Petitioners' behalf. *See* Silverman Report, filed as Ex. 72 June 17, 2019 (ECF No. 32-1) ("Silverman Rep."); Tr. at 4–55.

Dr. Silverman obtained his bachelor's degree in cellular biology and biochemistry from Revelle College at the University of California, San Diego before obtaining his medical degree

[7] S.M.'s positive Rhinovirus result is reported in the medical record, albeit briefly. Ex. 105 at 484.

from the University of California, San Diego School of Medicine. Silverman Curriculum Vitae, filed as Ex. 73 on June 17, 2019 (ECF No. 32-2) ("Silverman CV"). He completed an internal medicine internship before completing his residency in radiology, followed by several visiting fellowships in various subspecialties of radiology. *Id.* at 1–2. Dr. Silverman is board certified in radiology, but he does not hold certification in neuroradiology. *Id.* at 3; Tr. at 14, 44. Presently, Dr. Silverman serves as a clinical associate professor at the University of Southern California Keck School of Medicine. Silverman CV at 3. Over the course of his career, Dr. Silverman estimates that he has reviewed approximately 10,000 brain and spine images—though he admittedly reviews fewer pediatric studies now than in previously held positions. Tr. at 11, 15–16.

In preparing his opinions, Dr. Silverman reviewed MRI and CT[8] images obtained between July 2014 and May 2016, as well as the written reports for those images contained in the medical record. Tr. at 17. He concluded that S.M.'s radiological studies were all compatible with a TM diagnosis. *Id.* at 17–21; Silverman Rep. at 3.

Dr. Silverman explained how radiological evidence can help distinguish between TM and AFM diagnoses. Tr. at 23–24, 48. TM is characterized by "lesions extending for three or four spinal segments" and the area of signal intensity "generally involves more than two-thirds of the cross-sectional area of the spinal cord." *Id.* It is also common for TM to involve both gray and white matter. *Id.* at 24. This is in direct contrast to AFM, which is largely restricted to gray matter[9] of the anterior horn cells[10]—a feature that will appear as a "white butterfly" on T2-weighted MRIs—and extends only one or two levels. *Id.* at 24, 36, 41–42; *see also* B. Erlt-Wagner et al., *Acute Flaccid Myelitis in a 10-Year-Old Girl*, 290 Radiology 31, 31 (2019), filed as Ex. 78 on June 17, 2019 (ECF No. 32-7) (referring to Centers for Disease Control ("CDC") diagnostic criteria for AFM, including "MRI showing a spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments.") ("Erlt-Wagner"); E. Gordon-Lipkin et al., *Comparative Quantitative Clinical, Neuroimaging, and Functional Profiles in Children with Acute Flaccid Myelitis at Acute and Convalescent Stages of Disease*, 61 Developmental Medicine and Child Neurology 366, 371 (2019), filed as Ex. 124 on Jan. 16, 2020 (ECF No. 45-7) (concluding that the white matter of the spinal cord is largely spared abnormalities during both the acute and convalescent stages of AFM). Dr. Silverman also noted that AFM is quite rare, and thus physicians

[8] A computed tomography (CT) scan employs an emergent x-ray beam measured by a scintillation counter, with the results recorded and processed by a computer for reconstruction display. CT scans are useful when a disease of the central nervous system is implicated and degenerative abnormalities can be identified. Mosby's Manual of Diagnostic and Laboratory Tests 1026 (5th ed. 2014).

[9] On cross examination, Dr. Silverman clarified that AFM can also involve some white matter, but maintained that gray matter involvement tends to be far more extensive. Tr. at 51–52.

[10] Dr. Silverman acknowledge that during the acute stage of AFM, T2-weighted MRIs can show "ill-defined, abnormal, hyperintense signal…throughout the spinal cord gray matter," but will become better defined in the anterior horns of the gray matter as time progresses. Tr. at 51.

are much more likely to see cases of TM, even though the two can overlap somewhat in presentation. Tr. at 47.

By comparing S.M.'s radiological studies against these characteristics, Dr. Silverman concluded that S.M.'s presentation more closely aligned with that of TM. Tr. at 30. Notably, S.M. exhibited signal intensity spanning more than two-thirds of the cross-sectional area of her spinal cord, in addition to severe swelling and involvement of both gray and white matter. *Id.* (citing Ex. 132).

To further support his conclusion, Dr. Silverman compared S.M.'s imaging studies to those of known TM and AFM patients. Tr. at 34–35. Such a comparison revealed that S.M. shared several characteristics consistent with TM, including increased signal intensity through more than two-thirds of the cross-sectional area of the cord, gray and white matter involvement, and cord edema. *Id.* at 34 (*comparing* Illustrative Adult TM MRI, filed as Ex. 133 on Jan. 16, 2020 (ECF No. 46-6), *with* Ex. 132). When Dr. Silverman compared S.M.'s imaging results with those of a known AFM case, however, the hallmark "white butterfly" of AFM is notably absent from S.M.'s images. Tr. at 37 (*comparing* Illustrative Child AFM MRI, filed as Ex. 134 on Jan. 16, 2020 (ECF No. 46-7), *with* Ex. 132 at 4). Based upon these comparisons, Dr. Silverman concluded that S.M.'s radiological imaging studies were most consistent with a TM diagnosis. Tr. at 43.

2. Dr. Elizabeth Egan, M.D., Ph.D.

Dr. Egan, a pediatric infectious disease physician, provided three expert reports on Petitioners' behalf. Dr. Egan Report, filed as Ex. 23 on Apr. 13, 2018 (ECF No. 13-1) ("First Egan Rep."); Supplemental Report, filed as Ex. 46 on Nov. 30, 2018 (ECF No. 19-1) ("Second Egan Rep."); Second Supplemental Report, filed as Ex. 141 on July 29, 2020 (ECF No. 67-1) ("Third Egan Rep."). Based on her review of the medical records and hearing testimony, Dr. Egan concluded that S.M.'s TM was more likely than not caused by the third Hepatitis B vaccine dose that she received. *See* Third Egan Rep. at 7–8.

Dr. Egan received her bachelor's degree (biology) from Barnard College at Columbia University before obtaining both a medical degree and a Ph.D. in genetics from Tufts University. Elizabeth Egan Curriculum Vitae, filed as Ex. 24 on Apr. 13, 2018 (ECF No. 13-2). She completed an internship and residency in pediatrics at Boston Children's Hospital before completing fellowships in pediatric infectious disease and molecular parasitology at Boston Children's Hospital and the Harvard School of Public Health respectively. *Id.* at 1. Since 2015, Dr. Egan has served as an assistant professor at Stanford University School of Medicine where she teaches pediatrics, microbiology, and immunology. *Id.* She also works as an attending physician in pediatric infectious disease at Lucille Packard Children's Hospital in Stanford, California. *Id.* at 1.

Dr. Egan is board certified in pediatrics and pediatric infectious disease, and her research on subjects related to these fields has been published in several peer-reviewed journals. *Id.* at 2, 4–6.

Dr. Egan spent some time in her reports distinguishing AFM from TM. AFM, she explained, is characterized by hyporeflexia, intact sensation, pain in the affected limb, pleocytosis, and spinal cord lesions with primarily anterior horn involvement. Second Egan Rep. at 2 (citing J. Sejvar et al., *Acute Flaccid Myelitis in the United States, August – December 2014: Results of Nationwide Surveillance*, 63 Clinical Infectious Diseases 737, 737–45 (2016), filed as Ex. E on Aug. 21, 2018 (ECF No. 18-3); K. Messacar et al., *Enterovirus D68 and Acute Flaccid Myelitis – Evaluating the Evidence for Causality*, 18 Lancet e239, e239–47 (2018), filed as Ex. F on Aug. 21, 2018 (ECF No. 18-4) ("Messacar")). TM is a rare demyelinating condition that affects approximately 1-8 per million people in the United States, with twenty percent of cases occurring in children. First Egan Rep. at 6 (citing T.F. Scott et al., *Evidence Based Guideline: Clinical Evaluation and Treatment of Transverse Myelitis*, 77 Neurology 2128, 2128 (2011), filed as Ex. 26 on Apr. 13, 2018 (ECF No. 13-4)). TM is characterized by the "acute onset of motor, sensory, and/or autonomic dysfunction" due to a demyelinating lesion in the spinal cord. Third Egan Rep. at 2. Patients with TM may experience weakness, spasticity, pain, decreased sensation, and spinal cord edema involvement of both gray and white matter. *Id.*

Based on her review of the medical record and the entitlement hearing testimony of Drs. Silverman, Fantasia, and Yee, Dr. Egan noted that S.M. exhibited diffuse edema throughout her spinal cord, and there is no evidence to suggest that the spinal cord involvement was limited to the anterior horn cells as would be expected in AFM. Second Egan Rep. at 3. Additionally, S.M. did not experience hyporeflexia, nor did laboratory testing reveal evidence of an Enterovirus infection. *Id.* at 3–4; Third Egan Rep. at 3–7. Thus, Dr. Egan concluded that the evidence best supported S.M.'s initial diagnosis of TM. Second Egan Rep. at 4; Third Egan Rep. at 2–7.

Dr. Egan next evaluated the evidence supporting a causal relationship between TM and vaccines. While infections often precede its onset, there was literature support for vaccines also playing a causal role. One article found that twenty-eight percent of the studied TM patient subjects (13/47) had experienced symptoms onset within thirty days of receiving an immunization—with two of thirteen having received the Hepatitis B vaccine. First Egan Rep. at 6 (citing F.S. Pidcock et al., *Acute Transverse Myelitis in Childhood: Center-based Analysis of 47 Cases*, 68 Neurology 1474, 1476 (2007), filed as Ex. 27 on Apr. 13, 2018 (ECF No. 13-5) ("Pidcock"), at 1476). Additional literature offered by Dr. Egan also considered a possible association between vaccination and the development of TM, though none conclusively established a causal link. B. Banwell et al., *Incidence of Acquired Demyelination of the CNS in Canadian Children*, 72 Neurology 232, 232–38 (2009), filed as Ex. 28 on Apr. 13, 2018 (ECF No. 13-6); V. Wolf et al., *Pediatric Acute Transverse Myelitis Overview and Differential Diagnosis*, 27 J. Child Neurology 1426, 1426–36 (2012), filed as Ex. 29 on Apr. 13, 2018 (ECF No. 13-7).

Dr. Egan proposed molecular mimicry as the probable mechanism by which the Hepatitis B vaccine could cause TM. First Egan Rep. at 6–9. Her theory relied on homology between the Hepatitis B surface antigen, SHBsAg, and myelin basic protein ("MBP"). *Id.* at 7 (citing D. Bogdanos et al., *A Study of Molecular Mimicry and Immunological Cross-Reactivity Between Hepatitis B Surface Antigen and Myelin Mimics*, 12 Clinical & Developmental Immunology 217, 222 (2005), filed as Ex. 33 on Apr. 13, 2018 (ECF No. 14-1) ("Bogdanos")). Dr. Egan also identified myelin oligodendrocyte glycoprotein ("MOG") as a source of potential cross-reactivity. *Id.* at 7–8; Bogdanos at 222. Though Bogdanos did not find evidence of cross-reactivity between SHBsAg and MBP, reactivity to at least one MOG epitope was observed in sixty percent of study participants post-vaccination. Bogdanos at 220. This observation was deemed statistically significant, and according to Dr. Egan provided experimental evidence that antibodies produced in response to the Hepatitis B vaccine can cross-react with neural tissue resulting in demyelination. First Egan Rep. at 8.

Dr. Egan also identified several case reports describing instances of TM following receipt of the Hepatitis B vaccine. First Egan Rep. at 8 (citing L. Herroelen et al., *Central-Nervous-System Demyelination after Immunisation with Recombinant Hepatitis B Vaccine*, 338 Lancet 1174, 1174–75 (1991), filed as Ex. 37 on Apr. 13, 2018 (ECF No. 14-5) (reporting two cases of central nervous system ("CNS") demyelinating disease in patients within six weeks of receiving the recombinant Hepatitis B vaccine); E. Sindern et al., *Inflammatory Polyradiculoneuropathy with Spinal Cord Involvement and Lethal Outcome after Hepatitis B Vaccination*, 186 J. Neurological Sci. 81, 81–85 (2001), filed as Ex. 38 on Apr. 13, 2018 (ECF No. 14-6) (reporting a fatal case of inflammatory polyradiculoneuropathy in a thirty-six-year-old man nine days after he received the Hepatitis B vaccine); C. Vital et al., *Postvaccinal Inflammatory Neuropathy: Peripheral Nerve Biopsy in 3 Cases*, 7 J. Peripheral Nervous System: JPNS 163, 163–67 (2002), filed as Ex. 39 on Apr. 13, 2018 (ECF No. 14-7) (reporting two cases of inflammatory polyneuropathy within twenty-one days of receiving the Hepatitis B vaccine, and one case of an inflammatory polyneuropathy developing within fifteen days of receiving the yellow fever vaccine)).

Dr. Egan acknowledged that large epidemiological studies have not yet found an association between the Hepatitis B vaccine and demyelinating conditions. First Egan Rep. at 9 (citing A. Ascherio et al., *Hepatitis B Vaccination and the Risk of Multiple Sclerosis*, 344 New Eng. J. Med. 327, 327–32 (2001), filed as Ex. 40 on Apr. 13, 2018 (ECF No. 14-8); J. Mouchet et al., *Hepatitis B Vaccination and the Putative Risk of Central Demyelinating Diseases – A Systematic Review and Meta-Analysis*, 36 Vaccine 1548, 1548–55 (2018), filed as Ex. 41 on Apr. 13, 2018 (ECF No. 14-9); R. Baxter et al., *Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis*, 63 Clinical Infectious Diseases 1456, 1456–62 (2016), filed as Ex. 42 on Apr. 13, 2018 (ECF No. 14-10) ("Baxter")). But she deemed such studies to have limited value

due to the overall rarity of demyelinating conditions, while emphasizing case reports and the absence of other identifiable causes for S.M.'s condition. First Egan Rep. at 9–10.

3. Dr. Lawrence Steinman, M.D.

Dr. Steinman, a neurologist and immunologist, filed three expert reports. Report, dated Nov. 30, 2018, filed as Ex. 47 (ECF No. 19-2) ("First Steinman Rep."); Supplemental Report, dated Oct. 10, 2019, filed as Ex. 90 (ECF No. 34-1) ("Second Steinman Rep."); Supplemental Report, dated July 29, 2020, filed as Ex. 142 (ECF No. 67-2) ("Third Steinman Rep."). He opined—consistent with Dr. Egan—that the Hepatitis B vaccine S.M. received caused her to develop TM, although his focus was less on direct causation and more on other prongs of the test for entitlement.

Dr. Steinman currently serves as a professor in the departments of neurology, pediatrics, and genetics at Stanford University. Steinman Curriculum Vitae, filed as Ex. 97 (ECF No. 34-8) ("Steinman CV") at 1. He obtained his bachelor's degree from Dartmouth College before earning his medical degree from Harvard University. *Id.* He then completed his internship and residency in surgery, pediatrics, and pediatric and adult neurology at Stanford University. *Id.* He also completed several fellowships in the area of immunology. *Id.* He is board certified in neurology, though much of his work in the field also involves immunological concepts and theories. *Id.* at 2. He estimates that he has treated hundreds of patients with TM and other, similar neurological conditions, including multiple sclerosis and neuromyelitis optica throughout his career. Steinman Rep. at 1.

Regarding the competing diagnoses, Dr. Steinman opined (consistent with S.M.'s treaters plus Dr. Egan) that the evidence presented most strongly supported a diagnosis of TM. Third Steinman Rep. at 6–10. Relying on Dr. Silverman's hearing testimony, Dr. Steinman noted that the AFM diagnostic criteria set forth by the CDC requires a spinal cord lesion "largely restricted to gray matter," but that S.M.'s MRI demonstrated extensive involvement of both gray and white matter. *Id.* at 6–7 (citing Tr. at 41; Erlt-Wagner at 31). Dr. Steinman similarly deferred to Dr. Fantasia's opinions and her conclusion that S.M.'s clinical presentation was most consistent with TM. Third Steinman Rep. at 7 (citing Tr. at 114, 118–20). Though S.M.'s lumbar puncture did not reveal pleocytosis,[11] Dr. Steinman emphasized that negative CSF studies are not unusual and do not preclude a TM diagnosis. Third Steinman Rep. at 8–9. Yet because pleocytosis is more prevalent in AFM cases, its absence from S.M.'s CSF studies was actually further evidence of the unlikelihood of the proposed AFM diagnosis. *Id.* at 9.

[11] Pleocytosis describes the presence of greater than normal number of cells in cerebrospinal fluid. Dorland's at 1438.

According to Dr. Steinman, S.M. more likely than not developed TM as a result of the third Hepatitis B vaccine dose she received on July 14, 2014. Third Steinman Rep. at 12–13. To support his contention, Dr. Steinman highlighted several case reports and literature reviews describing instances in which patients developed TM or other demyelinating conditions following receipt of the Hepatitis B vaccine. *See, e.g.*, First Steinman Rep. at 4 (citing L. Fonesca et al., *Early-Onset Acute Transverse Myelitis Following Hepatitis B Vaccination and Respiratory Infection*, 61 Arq Neuropsiquiatr 265, 265–68 (2003), filed as Ex. 59 on Nov. 30, 2018 (ECF No. 20-4) (three-year-old boy experienced TM following an upper respiratory infection and vaccination with the Hepatitis B vaccine); Third Steinman Rep. at 3–4 (citing N. Agmon-Levin et al., *Transverse Myelitis and Vaccines: A Multi-Analysis*, 18 Lupus 1198, 1198–1204 (2009), filed as Ex. 111 on Jan. 16, 2020 (ECF No. 44-4) ("Agmon-Levin") (documenting thirteen cases of TM following receipt of the Hepatitis B vaccine between 1970 and 2009); J. Stübgen, *Immune-Mediated Myelitis Following Hepatitis B Vaccination*, 12 Autoimmunity Rev. 144, 144–49 (2012), filed as Ex. 113 on Jan. 16, 2020 (ECF No. 44-6) (identifying three more cases of TM following receipt of the Hepatitis B vaccine in addition to those described in Agmon-Levin, and noting that "HBV [Hepatitis B] vaccines were the most common immunization associated with acute myelitis.")). Dr. Steinman also cited the packaging insert for the Recombivax HB Hepatitis B vaccine, which lists TM as a reported adverse reaction. Third Steinman Rep. at 4 (citing Merk & Co., Inc., Recombivax HB Package Insert, 1, 5 (2018), filed as Ex. 112 on Jan. 16, 2020 (ECF No. 44-5)).

Dr. Steinman also addressed the science he felt supported the association of TM after receipt of the Hepatitis B vaccine. Like Dr. Egan, Dr. Steinman proposed that the mechanism by which S.M.'s TM could come have come about was molecular mimicry—cross-reactivity between antibodies produced in response to the Hepatitis B vaccine and the MBP found in the spinal cord, due to antigenic similarities between the amino acid sequences making up the MBP and vaccine components. Second Steinman Rep. at 4–6. As evidence of the potentiality of such mimicry, Dr. Steinman turned to the National Institutes of Health Immune Epitope Database, which he maintained revealed a shared epitope[12] between the Hepatitis B virus surface antigen (SHBsAg) and MBP. *Id.*

Dr. Steinman further bulwarked his theory with reference to an animal-model study in which researchers found that this shared homology had elicited a pro-inflammatory response and cytotoxicity. Second Steinman Rep. at 5 (citing S. Ellmerich et al., *High Incidence of Spontaneous Disease in an HLA-DR15 and TCR Transgenic Multiple Sclerosis Model*, 174 J. Immunology 1938, 1938, 1944–45 (2005), filed as Ex. 94 on Oct. 10, 2019 (ECF No. 34-5)). In addition, pro-inflammatory cytokines—specifically gamma interferon—stimulated during the innate response to vaccination can increase permeability of the blood-brain barrier, thereby allowing cytotoxic T-cells access to the CNS. Second Steinman Rep. at 5–6 (citing L. Steinman, *A Brief History of T_H17, the First Major Revision in the T_H1/T_H2 Hypothesis of T-Cell Mediated Tissue Damage*, 13 Nature

[12] An epitope is an antigenic determinant. Dorland's at 630.

Medicine 139, 143 (2007), filed as Ex. 95 on Oct. 10, 2019 (ECF No. 34-6)). This made it more likely that the secondary, pathologic adaptive response that was key to Dr. Steinman's theory could come about.

The larger focus of Dr. Steinman's reports, however, was his contention that the timeframe in which S.M.'s TM manifested post-vaccination was medically reasonable. S.M. experienced onset of her TM approximately seventy-seven hours (three days and five hours) after receiving her third dose of the Hepatitis B vaccine. Third Steinman Rep. at 13. As a general rule, the expected lag phase post-vaccination (when B and T cells are activated and differentiate into effector and memory cells) would be between one to three days, with the logarithmic phase—the period during which serum antibody levels increase—then occurring in the following three to five days. First Steinman Rep. at 4 (citing K. Stratton et al., *Adverse Effects of Vaccines: Evidence and Causality*, Institute of Medicine 58 (2012), filed as Ex. 56 on Nov. 30, 2018 (ECF No. 20-1) ("IOM Rep.")). However, since S.M. had been exposed to the Hepatitis B vaccine twice before, she would likely mount an adaptive response to the third dose of the same vaccine in an even shorter amount of time. First Steinman Rep. at 4. Thus, the onset of S.M's symptoms approximately three days post-vaccination was medically acceptable in his view.

C. *Respondent's Experts*

1. Dr. Margaret Fisher, M.D.

Dr. Fisher, a pediatric infectious disease physician, offered four reports in support of Respondent's position. Expert Report, filed as Ex. A on July 30, 2018 (ECF No. 17-1) ("First Fisher Rep."); Supplemental Expert Report, filed as Ex. G on Mar. 8, 2019 (ECF No. 29-1) ("Second Fisher Rep."); Second Supplemental Expert Report, filed as Ex. Z on Dec. 16, 2019 (ECF No. 40-7) ("Third Fisher Rep."); Third Supplemental Expert Report, filed as Ex. EE on Sept. 14, 2020 (ECF No. 68-1) ("Fourth Fisher Rep."). Based upon her review of the medical record, scientific literature, expert reports, and entitlement hearing testimony, Dr. Fisher concluded that S.M. more likely than not suffered from AFM, and she attributed the AFM to a preceding infection rather than vaccination. First Fisher Rep. at 5.

Dr. Fisher obtained her bachelor's degree (chemistry) from the Susquehanna University in Pennsylvania before obtaining her medical degree from the University of California, Los Angeles. Dr. Fisher Curriculum Vitae, filed as Ex. B on July 30, 2018 (ECF No. 17-2). She then completed her residency in pediatrics and a fellowship in pediatric infectious disease at St. Christopher's Hospital for Children in Philadelphia, Pennsylvania. *Id.* at 2. Dr. Fisher is a professor of pediatrics at both Drexel University College of Medicine and St. George's University School of Medicine. *Id.* In addition to her teaching duties, Dr. Fisher serves as an attending pediatric physician and medical director at Unterberg Children's Hospital at Monmouth Medical Center. *Id.* at 4. She is

board certified in both pediatrics and pediatric infectious disease, and she has published journal articles and lectured on these topics extensively. *Id.* at 12–47.

In her first report, Dr. Fisher described the AFM outbreak that occurred in the Summer of 2014—the exact period relevant to this case. First Fisher Rep. at 3–4. Citing to CDC advisories and reports, Dr. Fisher described sixty-four cases of "acute onset of limb weakness in a person less than or equal to 21 years of age with onset on or after 01 August, 2014, and with spinal MRI lesions largely restricted to the spinal grey matter." *Id.* at 3 (citing Centers for Disease Control and Prevention, *Acute Neurological Illness with Focal Limb Weakness of Unknown Etiology in Children*, CDC Health Alert Network (Sept. 26, 2014), filed as Ex. C on Aug. 21, 2018 (ECF No. 18-1); Centers for Disease Control and Prevention, *Acute Flaccid Myelitis: Interim Considerations for Clinical Management* (Nov. 7, 2014), filed as Ex. D on Aug. 21, 2018 (ECF No. 18-2) ("CDC Clinical Management")). She also emphasized that the majority of patients presenting with AFM were experiencing severe respiratory illness, and in some cases required ventilation for respiratory failure. First Fisher Rep. at 3. While corticosteroid treatment was recommended for cases in which spinal cord edema was likely to result in additional damage, neither it nor PLEX were recommended for treatment of AFM. *Id.* (citing CDC Clinical Management at 6, 8). It was later determined that a causal association existed between enterovirus infections—specifically EV-D68 infections—and the development of AFM. First Fisher Rep. at 4 (citing Messacar at e245).

Though acknowledging that differentiating between a diagnosis of AFM and TM is difficult, Dr. Fisher ultimately concluded that the medical record suggested that S.M. more likely than not suffered from AFM. First Fisher Rep. at 5; Second Fisher Rep. at 2–3. First, Dr. Fisher observed symptoms and treatment evidence from the medical record that she maintained were more consistent with AFM. First Fisher Rep. at 3. She noted that S.M. experienced symptoms of an upper respiratory infection approximately three weeks prior to the onset of her condition—a timeframe consistent with the pathogenesis of AFM following an enterovirus infection. *Id.*; Third Fisher Rep. at 1. She also emphasized S.M.'s limited improvement despite corticosteroid treatment. First Fisher Rep. at 2–3. Similarly, S.M.'s condition did not show significant improvement with PLEX treatment. *Id.*

Second, Dr. Fisher noted that the circumstances of S.M.'s symptoms manifestation were inconsistent with TM—but consistent with AFM. According to Dr. Fisher, the time between S.M.'s receipt of the Hepatitis B vaccine and the onset of her condition was too brief for molecular mimicry to have occurred. First Fisher Rep. at 5. By contrast, about half of AFM cases occurred after "an infectious illness at an average of 11 ± 10 days prior to the onset of neurologic symptoms." *Id*. at 4 (citing Pidcock at 1476). The onset of S.M.'s symptoms three weeks after she was seen by her pediatrician for an upper respiratory illness would thus be consistent with a post-infectious AFM diagnosis. First Fisher Rep. at 4–5.

Dr. Fisher also identified a preceding enterovirus infection as the most likely etiology for S.M.'s condition. First Fisher Rep. at 4–5. To support her position, she again referenced the pediatrician visit on June 20, 2014, three weeks prior to the onset of S.M.'s neurologic symptoms. First Fisher Rep. at 4. During the visit, S.M. was evaluated for congestion, yellow nasal discharge, and a fever for which she was prescribed oral antibiotics (amoxicillin). *See* Ex. 7 at 104. And S.M. appeared to show respiratory difficulties the evening before and morning of her first hospital admission. First Fisher Rep. at 4. While Petitioners attributed these symptoms to S.M.'s allergies, Dr. Fisher opined that they were also consistent with an enterovirus infection. *Id.*

Dr. Fisher also pointed out the positive rhinovirus finding on S.M.'s respiratory panel workup as consistent with an enterovirus infection, because rhinovirus and enterovirus are cross-reactive. First Fisher Rep. at 2. And even if S.M.'s respiratory panel accurately reflected a rhinovirus rather than an enterovirus infection, it was still possible that her AFM stemmed from an infectious etiology because most AFM cases "have not had a specific viral pathogen identified." Second Fisher Rep. at 3 (citing M. Elrick et al., *Clinical Subpopulations in a Sample of North American Children Diagnosed with Acute Flaccid Myelitis, 2012-2016*, 173 JAMA Pediatrics 134, 137 (2019), filed as Ex. H on Mar. 8, 2019 (ECF No. 29-2)); *see also* Third Fisher Rep. at 2–3.

2. Dr. Ross Kedl, Ph.D.

Dr. Kedl, a professor of immunology at the University of Colorado, offered three expert reports on Respondent's behalf. Expert Report, filed as Ex. K on Mar. 8, 2019 (ECF No. 29-5) ("First Kedl Rep."); Supplemental Report, filed as Ex. T on Dec. 16, 2019 (ECF No. 40-1) ("Second Kedl Rep."); Supplemental Report, filed as Ex. FF on Sept. 14, 2020 (ECF No. 68-2) ("Third Kedl Rep."). Based upon his review of the medical record, scientific literature, expert reports, and entitlement hearing testimony, Dr. Kedl concluded that S.M.'s illness, however characterized—though he largely deferred to Dr. Fisher on this point and agreed with her opinion that S.M. more likely than not suffered from AFM—was not caused by the Hepatitis B vaccine. First Kedl Rep. at 8–9.

Dr. Kedl received both his bachelor's degree in biology and Ph.D. in pathobiology from the University of Minnesota. Ross Kedl Curriculum Vitae, filed as Ex. L on Mar. 8, 2019 (ECF No. 29-6). He then completed a post-doctoral fellowship at the Howard Hughes Medical Institute in Denver, Colorado. *Id.* at 1. Since 2004, Dr. Kedl has served as a professor of immunology at the University of Colorado Department of Immunology and Microbiology. *Id.* at 3. He is a co-author of several patents relating to vaccine development and immunological modifiers. *Id.* at 4–5. Much of Dr. Kedl's research has been focused on vaccine development and the role of vaccine adjuvants in stimulating immunologic responses, and he is extensively published on these and related subjects. *Id.* at 11–19; *see also* First Kedl Rep. at 2. Dr. Kedl does not, however, possess a

medical degree, nor does he have medical experience in treating or diagnosing patients with infectious or neurological disease.

Deferring to Dr. Fisher's opinions regarding S.M.'s diagnosis,[13] Dr. Kedl's first report largely focused on possible alternative etiologies for S.M.'s condition. He began by explaining how the two arms of the immune system—humeral and cellular immunity—operate during an adaptive immune response. First Kedl Rep. at 4–5. According to Dr. Kedl, cellular immunity is driven by T cell activity, while humeral immunity (implicated in a causal theory like molecular mimicry) relies on B cell antibody production. *Id.* at 4. During an initial exposure to an antigen, both CD4+/helper T cells and CD8+/cytotoxic T cells migrate from lymphoid tissue to the infection site. During the same initial exposure, B cells increase antibody production while remaining localized in lymphoid tissue and bone marrow. *Id.* Once the infection is cleared, some T cells will remain present in the formerly-infected tissue, and are thereafter referred to as resident memory T cells. *Id.* Other T cells will recirculate throughout the body, serving as monitors for future infections. *Id.* These T cells are referred to as central memory T cells. *Id.* It is these memory T cells which allow for a faster immunologic response to subsequent infections. *Id.* While the response of B cells to subsequent infection will also be accelerated, it remains delayed relative to the T cell response. *Id.* (citing IOM Rep. at 57–58).

Based on the foregoing, Dr. Kedl concluded that:

> activation of adaptive immunity in less than 3 days requires the existence of immune memory, [ ] immune-mediated tissue disruption within this timeframe requires memory T cell residence within, or entrance into, the tissue site of interest, and [ ] antibody-mediated tissue damage would be expected to take longer than 3 days and would still require the previous generation of memory T cells.

First Kedl Rep. at 5.

During his review of the medical record—specifically S.M.'s pathology and laboratory studies—Dr. Kedl highlighted certain results he deemed antithetical to the conclusions of Petitioners' causation experts. First Kedl Rep. at 5. First, he noted that the results of S.M.'s CSF study on July 14, 2014 revealed elevated albumin, IgG, and red blood cells, but did not show white blood cell infiltrate. *Id.* (citing Ex. 4 at 64–65). This finding, according to Dr. Kedl, is "consistent with damage to the blood-CSF barrier, but not with T cell infiltration or associated tissue damage." First Kedl Rep. at 5. Because the formation of memory B cells is a T cell-dependent event, the absence of T cell expansion across the blood-brain barrier similarly precludes B cell—and later,

[13] From an immunologic perspective, Dr. Kedl noted that S.M.'s rhinovirus infection and the lack of cellular infiltrates in her CSF studies were most consistent with Dr. Fisher's proposed AFM diagnosis. First Kedl Rep. at 4.

antibody—access to CNS tissue. *Id.* Dr. Kedl thus rejected Dr. Steinman's contention that the third dose of a Hepatitis B vaccine could have elicited a secondary T and B cell response sufficient to cause CNS tissue damage in the timeframe at issue—but remain undetectable in CSF studies. Second Kedl Rep. at 2–3; Third Kedl Rep. at 4–5.

Dr. Kedl next addressed other specific aspects of the molecular mimicry theory proposed by Dr. Steinman. First Kedl Rep. at 5–6; Second Kedl Rep. at 4–6. He emphasized that sequential homology is quite common, and is thus (in his view) insufficient to establish the likelihood of cross-reactivity. Second Kedl Rep. at 4–5 (citing A. Silvanovich et al., *The Value of Short Amino Acid Sequence Matches for Prediction of Protein Allergenicity*, 90 Toxicological Sciences 252, 252 (2006), filed as Ex. X on Dec. 16, 2019 (ECF No. 40-5) ("Silvanovich")). Significantly, Dr. Kedl highlighted that PADPGSRP—the amino acid sequence Dr. Steinman identified as the source of homology between MBP and SHBsAg—is not actually found in SHBsAg. Second Kedl Rep. at 4. Even after Dr. Steinman revised his opinion—identifying PADPGSRPHLIRLF as the amino acid sequence giving rise to cross-reactivity—Dr. Kedl opined that the fifty-seven percent similarity between this sequence and SHBsAg sequences remained insufficient to establish a causal association between the Hepatitis B vaccine and TM. Third Kedl Rep. at 5–7 (citing Bogdanos at 219; Silvanovich at 252).

Dr. Kedl further criticized reliance on case reports to establish a causal relationship between the Hepatitis B vaccine and TM, especially given the existence of several reliable epidemiological studies which reached the opposite conclusion. First Rep. at 6–7 (citing Baxter (also filed by Respondent as Ex. M); *see also* M. Hocine et al., *Hepatitis B Vaccination and First Central Nervous System Demyelinating Events: Reanalysis of a Case-Control Study Using the Self-Controlled Case Series Method*, 25 Vaccine 5938, 5938–43 (2007), filed as Ex. P on Mar. 8, 2019 (ECF No. 29-10) ("Hocine"); A. Schattner, *Consequence or Coincidence? The Occurrence, Pathogenesis and Significance of Autoimmune Manifestations after Viral Vaccines*, 23 Vaccine 3876, 3876–86 (2005), filed as Ex. S on Mar. 8, 2019 (ECF No. 29-13) ("Schattner")).

III. Procedural History

After the case's commencement in 2017, Petitioners filed medical records in support of their claim. Respondent thereafter filed a Rule 4(c) Report on January 19, 2018, asserting that compensation was not appropriate in this case. Respondent's Report, filed Jan. 19, 2018 (ECF No. 10). Petitioners subsequently filed expert reports from Drs. Egan, Steinman, and Silverman along with supporting literature and reports from treaters, including Drs. Fantasia and Bal, between the spring of 2018 and winter 2020. Respondent filed responsive reports from Drs. Fisher and Kedl, along with literature in opposition to Petitioners' position. A two-day entitlement hearing was scheduled to take place on January 28-29, 2020. *See* Scheduling Order, dated Dec. 6, 2019.

On January 22, 2020, it was brough to my attention that Respondent's counsel was ill and would require special accommodation for the upcoming entitlement hearing. *See* Scheduling Order, dated Jan. 22, 2020. The parties therefore agreed that only Drs. Silverman, Yee, and Fantasia, along with both Mr. and Mrs. McGrail, would testify at the time originally set for the hearing. *See* Scheduling Order, dated Jan. 22, 2020. All other witnesses were to testify during two additional days of hearing on June 10-11, 2020. *See* Scheduling Order, dated Jan. 31, 2020 (ECF No. 56). On May 1, 2020, however, the parties indicated that they no longer wished to proceed with the additional days of entitlement hearing testimony, and were instead amenable to the case being resolved on the existing record. Joint Status Report, filed May 1, 2020 (ECF No. 65). Thereafter, the parties submitted briefs in support of their respective positions, concluding the process on November 13, 2020. The matter is now ripe for resolution.

IV. Parties' Respective Arguments

A. *Petitioner's Motion*

Petitioners argue that S.M. developed TM after receiving the third dose of the Hepatitis B vaccine on July 14, 2014. Motion for Ruling on the Record, filed on Nov. 13, 2020 (ECF No. 70) ("Mot.") at 8. Relying on the reports of Drs. Steinman, Egan, and Silverman, in addition to the medical literature and testimony of treating physicians, Petitioners posit that sequential homologies in amino acid sequences of Hepatitis B vaccine components and MBP allowed for cross-reactivity, leading to demyelination of the spinal cord and resulting in an acute onset of TM. *Id.* at 40–43.

Petitioners specifically contend that the onset of S.M.'s condition occurred on July 17, 2014—approximately seventy-seven hours after receiving her third dose of the Hepatitis B vaccine. Mot. at 56–69. That morning, S.M.'s parents noted that she was exhibiting allergy symptoms (shortness of breath and coughing), for which they administered a Pulmicort nebulizer treatment. Tr. at 143–44; Ex. 5 at 32. S.M.'s parents described S.M. as otherwise healthy and behaving normally prior to her being taken to daycare. Mot. at 19–20. It wasn't until approximately 3:00 in the afternoon that Ms. McGrail was informed by S.M's daycare that she had developed a fever and needed to be picked up. *Id.* at 20; Tr. at 162. At the recommendation of S.M.'s pediatrician, Dr. Yee, S.M. was taken to the local emergency department for further evaluation of her symptoms. Mot. at 11.

Upon admission to Jersey Shore University Medical Center, S.M. underwent a spinal MRI which produced results deemed most consistent with TM. Mot. at 12 (citing Ex. 4 at 28–29). CSF studies performed that same evening were negative for pleocytosis, but did reveal elevated IgG. Mot. at 52, 62 (citing Ex. 4 at 64–65). Based on S.M.'s clinical presentation and the results of both her MRI and CSF studies, her treating neurologist, Dr. Sultan, diagnosed her with TM. Mot. at 23–24 (citing Ex. 105 at 479–80).

Between July 17 and August 14, 2014, S.M. received steroid and PLEX treatments before being transferred to Children's Specialized Hospital for intensive inpatient physical therapy. Mot. at 13–14. After a month of inpatient rehabilitation, S.M. was discharged from Children's Specialized Hospital and was instructed to follow-up with her treating physiatrist, Dr. Fantasia. *Id.* at 15. S.M. continued with outpatient physical, occupational, and speech therapies, but she still experiences residual sequelae, including severe spasticity, neuromuscular derangements, bladder dysfunction, bowel dysfunction, extremities contracture, orthopedic complications, and other issues related to quadriplegia. *Id.* at 1.

It was not until S.M. was evaluated by Dr. Waldman on January 7, 2017—more than two years after the onset of her condition—that AFM was raised as a possible diagnosis. Mot. at 33. But even as she acknowledged that the onset and clinical course of S.M.'s condition appeared consistent with AFM, Dr. Waldman's visit notes document an encounter diagnosis of TM. Ex. 14 at 5.

B. *Respondent's Opposition*

Respondent first disputes Petitioners' proposed TM diagnosis, arguing instead that S.M. suffers from post-infectious AFM. Respondent's Opposition Brief, filed Nov. 13, 2020 (ECF No. 69) ("Opp.") at 6, 8–9. Dr. Fisher, Respondent's pediatric infectious disease expert, opined that S.M.'s clinical presentation of cough, fever, acute onset quadriparesis, spinal cord inflammation, and limited improvement after steroid and PLEX treatments are most consistent with a diagnosis of AFM. *Id.* at 9. She also identified the positive rhinovirus culture obtained on August 1, 2014 as evidence of AFM because the respiratory panel culture does not distinguish between rhinovirus and enterovirus, and both infections have been associated with the development of AFM. *Id.*

Moreover, even if S.M.'s initial TM diagnosis was correct, Petitioners have failed to preponderantly establish causation under *Althen*. Opp. at 10. Respondent's immunology expert, Dr. Kedl, identified several flaws in the proposed theory of causation. *Id.* at 12. First, the amino acid sequence identified as the source of cross-reactivity is not actually found in the Hepatitis B vaccine antigen, and the vaccine antigen sequence with the highest degree of similarity to those found in MBP contains only four shared amino acids. *Id.* Dr. Kedl emphasized that this degree of similarity is quite common throughout the human genome and can occur by random chance, and even significant degrees of similarity do not inevitably cause meaningful pathology. *Id.* at 13. He also noted that even an adaptive immune response would not be capable of producing antibody-mediated damage to the spinal cord within the three-day timeframe proposed by Petitioners. *Id.*

Respondent also contends that Petitioners failed to satisfy their burden in establishing a logical sequence of cause and effect showing that the Hepatitis B vaccine was the likely source of S.M.'s injury as is required by the second *Althen* prong. Opp. at 13. According to Dr. Kedl, if

cross-reactivity were implicated in the pathological processes leading to the development of TM, certain clinical markers would be present. *Id.* But CSF studies performed within hours of S.M.'s symptom onset did not reveal evidence of pleocytosis, and were therefore inconsistent with T cell infiltration and damage to the spinal cord. *Id.*

The final criticism offered by Respondent emphasized a lack epidemiological evidence supporting Petitioners position. Opp. at 14–15. Though a number of case reports documenting instances of TM following close in time to receipt of the Hepatitis B vaccine have been offered, Respondent downplays their overall significance in light of several epidemiological studies which found no association between the Hepatitis B vaccine and TM. *Id.*

V. Applicable Legal Standards

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[14] In this case, Petitioners do not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Hum. Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions;

[14] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen*, 418 F.3d at 1278: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury."

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras*, 121 Fed. Cl. at 245 ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)).

In discussing the evidentiary standard applicable to the first *Althen* prong, the Federal Circuit has consistently rejected the contention that it can be satisfied merely by establishing the proposed causal theory's scientific or medical *plausibility*.[15] *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); *see also LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[h]owever, in the past we have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." (citing *Moberly*, 592 F.3d at 1322)). And petitioners always have the ultimate burden of establishing their *overall* Vaccine Act claim with preponderant evidence. *W.C. v. Sec'y*

[15] Petitioners are thus consistently in error when they maintain the legal standard requires only plausibility. *See, e.g.*, *Boatmon*, 746 F.3d at 1359. However, because Petitioners also maintain (and in my determination, have demonstrated) that the evidence preponderantly establishes the "can cause" prong, this misstatement of the legal standard is not fatal to Petitioners' overall success.

of Health & Hum. Servs., 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed. Cl. 782, 793 (2017) (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Medical records and statements of a treating physician, however, do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Hum. Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Dept. of Health & Hum. Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review denied*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. Appx. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum.*

Servs., 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for rev. denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Legal Standards Governing Factual Determinations*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd sub nom. Rickett v. Sec'y of Health & Hum. Servs*., 468 F. Appx. 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie*, 2005 WL 6117475, at *20. Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral

testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy*, 23 Cl. Ct. at 733 (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

There are, however, situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("'[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent'") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs*., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *Lalonde v. Sec'y of Health & Hum. Servs*., 110 Fed. Cl. 184, 203-04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999)). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a

theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for rev. denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. Appx. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

Expert opinions based on unsupported facts may be given relatively little weight. *See Dobrydnev v. Sec'y of Health & Hum. Servs.*, 556 F. Appx. 976, 992–93 (Fed. Cir. 2014) ("[a] doctor's conclusion is only as good as the facts upon which it is based") (citing *Brooke Group Ltd.*

v. Brown & Williamson Tobacco Corp., 509 U.S. 209, 242 (1993) ("[w]hen an expert assumes facts that are not supported by a preponderance of the evidence, a finder of fact may properly reject the expert's opinion")). Expert opinions that fail to address or are at odds with contemporaneous medical records may therefore be less persuasive than those which correspond to such records. *See Gerami v. Sec'y of Health & Hum. Servs.*, No. 12-442V, 2013 WL 5998109, at *4 (Fed. Cl. Spec. Mstr. Oct. 11, 2013), *aff'd*, 127 Fed. Cl. 299 (2014).

D. *Consideration of Medical Literature*

Both parties filed medical and scientific literature in this case, but not every filed item factors into the outcome of this decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.,* 527 F. Appx. 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

E. *Consideration of Comparable Special Master Decisions*

In reaching a decision in this case, I have considered other decisions issued by special masters (including my own) involving similar injuries, vaccines, or circumstances. I also reference some of those cases in this Decision, in an effort to establish common themes, as well as demonstrate how prior determinations impact my thinking on the present case.

There is no error in doing so. It is certainly correct that prior decision in different cases do not *control* the outcome herein.[16] *Boatmon,* 941 F.3d at 1358-59; *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). Thus, the fact that another special master reasonably determined elsewhere, on the basis of facts not in evidence in this case, that preponderant evidence supported the conclusion that vaccine X caused petitioner's injury Y does not compel me to reach the same conclusion in *this* case. Different actions present different background medical histories, different experts, and different items of medical literature, and therefore can reasonably result in contrary determinations.

[16] By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014). Special masters are also bound within a specific case by determinations made by judges of the Court of Federal Claims after a motion for review is resolved.

However, it is *equally* the case that special masters draw upon their experience in resolving Vaccine Act claims. *Doe v. Sec'y of Health & Hum. Servs.,* 76 Fed. Cl. 328, 338-39 (2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the *expertise and experience to know the type of information that is most probative of a claim*") (emphasis added). They would therefore be remiss in ignoring prior cases presenting similar theories or factual circumstances, along with the reasoning employed in reaching such decisions. This is especially so given that special masters not only routinely hear from the same experts in comparable cases but are also repeatedly offered the *same* items of medical literature regarding certain common causation theories. It defies reason and logic to obligate special masters to "reinvent the wheel", so to speak, in each new case before them, paying no heed at all to how their colleagues past and present have addressed similar causation theories or fact patterns. It is for this reason that prior decisions can have high persuasive value—and why special masters often explain how a new determination relates to such past decisions.[17] Even if the Federal Circuit does not *require* special masters to distinguish other relevant cases (*Boatmon,* 941 F.3d at 1358), it is still *wise* to do so.

F. *Determining Matter on Record Rather Than at Hearing*

After conducting the first part of a planned multi-day hearing, the parties consented to having this case decided based on written submissions and evidentiary filings, including the numerous expert reports that have been submitted. The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions (or components of a claim) on the papers rather than via evidentiary hearing, where (in the exercise of their discretion) they conclude that the former means of adjudication will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The Federal Circuit has recently affirmed this practice. *Kreizenbeck v. Sec'y of Health & Hum. Servs.*, 945 F.3d 1362, 1365–66 (Fed. Cir. 2020). It simply is not the case that every Vaccine Act claim need be resolved by hearing—even where the petitioner explicitly so requests.

ANALYSIS

I. *Prior Decisions Involving TM and the Hepatitis B Vaccine*

Claims alleging acute demyelinating conditions, like TM, following vaccination are common in the Vaccine Program—and many have met with success. *Compare Palattao v. Sec'y of Health & Hum. Servs.*, No. 13-591V, 2019 WL 989380 (Fed. Cl. Spec. Mstr. Feb. 4, 2019)

[17] Consideration of prior determinations is a two-way street that does not only inure to the benefit of one party. Thus, I would likely take into account the numerous decisions finding no association between vaccination and autism when confronted with a new claim asserting autism as an injury, and I have informed such claimants early in the life of their case that the claim was not viable for just that reason. But I would *also* deem a non-Table claim asserting GBS after receipt of the flu vaccine as not requiring extensive proof on *Althen* prong one "can cause" matters, for the simple reason that the Program has repeatedly litigated the issue in favor of petitioners.

(denying entitlement for a claim alleging TM following receipt of several vaccines in an infant child who experienced onset between thirty and thirty-six hours after vaccination), *with Pearson v. Sec'y of Health & Hum. Servs.*, No. 03-2751V, 2008 WL 5093378 (Fed. Cl. Spec. Mstr. Nov. 6, 2008) (finding in favor of a petitioner who alleged TM as a result of the Hepatitis B vaccine). Often the nature of the causal theory proposed has made the difference in whether the claimant was found entitled to damages. *See Palattao*, 2019 WL 989380, at *8 n.10 (denying entitlement for petitioners who asserted that pathological demyelination was the result solely of the innate immune system inducing an overwhelming proinflammatory cytokine response); *Stevens v. Sec'y of Health & Hum. Servs.*, No. 99-594V, 2006 WL 659525, at *1, 25 (Fed. Cl. Spec. Mstr. Feb. 24, 2006) (granting entitlement in favor of a petitioner who asserted a theory of challenge/rechallenge). While these decisions do not bind this determination, I take note of them and their sound analyses.

In the present matter, Petitioners' experts propose molecular mimicry as the causal mechanism by which the Hepatitis B vaccine can cause TM—a theory distinguishable from what was relied upon in other cases involving the same injury. For example, the petitioners in *Palattao* (who also alleged an infant's TM was vaccine-caused) expressly *rejected* the theory of molecular mimicry espoused in this case, relying instead solely on an aberrant proinflammatory cytokine response as the disease driver. *Id.* at *8. I found that the petitioners had failed to "demonstrate that cytokine upregulation in the periphery attributable to a vaccine can *also* trigger TM." *Id.* at *36 (emphasis in original).

In *Stevens*, the special master determined that the petitioner was entitled to compensation for TM she developed subsequent to receiving two doses of the Hepatitis B vaccine. *Stevens*, 2006 WL 659525, at *25. Unlike the present case, however, the petitioner in *Stevens* successfully demonstrated that her adverse reaction was due to a challenge/re-challenge rather than cross-reactivity. *Id.* at *1. And in *Pearson*, the special master did not identify the proposed causal theory at all, but instead relied on her prior ruling in *Stevens* to conclude that the Hepatitis B vaccine can cause TM. *Pearson*, 2008 WL 5093378, at *3. These cases demonstrate that the evidentiary value and persuasiveness of the causal theory can vary from case to case—resulting in disparate outcomes even though vaccine and injury are the same.

II. *Petitioners Have Established TM as S.M.'s Injury*

In many cases, the first step in deciding a claim is to determine the nature of the petitioner's injury—especially if the causal theory is dependent on establishing that a specific injury occurred. *Broekelschen*, 618 F.3d at 1345; *LaPierre v. Sec'y of Health & Hum. Servs.*, No. 17-227V, 2019 WL 6490730, at *16–17 (Fed. Cl. Spec. Mstr. Oct. 18, 2019). That is the case here, since the parties strenuously dispute the proper diagnosis—TM or AFM—and since Petitioners' causation theory wholly assumes that the former to be the correct one. Petitioners have *not* alleged that AFM

could be vaccine-caused, so a determination that this best characterized S.M.'s injury would be fatal to their claim.

Ample evidence from the medical record supports Petitioners' allegation that TM best characterizes S.M.'s injury. Of great significance is the fact that S.M.'s initial treating physicians deemed her clinical presentation consistent with TM. That diagnosis was largely based on imaging and laboratory studies conducted within hours of her symptom onset, as well as findings present on physical examination. *See* Bal Rep.; Ex. 4 at 28; Ex. 5 at 19–21, 83–86. Petitioners also specifically note that the MRI conducted on July 17, 2014, revealed inflammation spanning the levels of C2 through T6 and affecting both the gray and white matter of the spinal cord. Ex. 4 at 28. These findings were initially interpreted as being consistent with TM, and this interpretation was later confirmed by the opinion of Petitioners' radiology expert, Dr. Silverman. *Id.*; Silverman Rep. at 3; Tr. at 30. Dr. Bal, S.M.'s treating infectious disease specialist, agreed with the TM diagnosis, and he noted that CSF studies showing an elevated IgG index were consistent with spinal cord inflammation. Bal Rep. at 2. The medical record is otherwise replete with evidence that S.M. was experiencing motor, sensory, and autonomic dysfunction—all of which are more characteristic of TM than AFM. *See* Ex. 105 at 17–18, 21, 25, 27–28.

The context in which AFM arose as a potential counter-diagnosis is also relevant. Not until January 2017—more than two years after the initial onset of S.M.'s symptoms— did any of S.M.'s treaters consider the possibility of AFM. Ex. 14 at 5. But even then, S.M.'s TM diagnosis remained unchanged. *Id.* And while the delay in proposing this alternative diagnosis could be credited to the fact that the AFM "outbreak" occurred in 2014 (the time period at issue here), it remains the case that substantial record evidence is wholly consistent with the conclusion that S.M.'s injury was TM. Although it is always reasonable when evaluating a medical record in hindsight to take into account subsequent medical information that may not have been known at the time, the mere fact that an AFM outbreak was temporally congruent with the onset of S.M.'s symptoms does not mean that she suffered from AFM per se. Here, it is reasonable to infer from this record that the timing of S.M.'s symptoms onset was the main driver for the proposed alternative diagnosis.

Respondent did cite some record evidence to rebut Petitioners' proffered TM diagnosis independent of the AFM outbreak. Dr. Kedl credibly noted that CSF studies conducted upon S.M.'s admission on July 17, 2014 did not reveal pleocytosis—contrary to what would be expected for TM (although its absence also further reduced the explanatory power of the alternative AFM diagnosis). First Kedl Rep. at 1, 5. And S.M.'s condition did not significantly improve with steroid or PLEX treatments, as would have been expected if she suffered from TM. First Fisher Rep. at 3–4. Beyond that, the respiratory panel results indicated S.M. was experiencing a rhinovirus infection close in time to the onset of her condition—and as Dr. Fisher noted, rhinovirus and enterovirus may cross-react during the respiratory panel study. *Id.* at 4. If S.M. was in fact suffering from an enterovirus rather than a rhinovirus infection, this would lend support to Respondent's

AFM diagnosis, because there is a known association between enterovirus—specifically the EV-D68 strain—and the development of AFM. *Id.*

Weighing all of the above, I find that record preponderates in Petitioners' favor on the contention that S.M.'s condition is best understood as TM rather than AFM. In reaching this conclusion, I note that the opinions offered by S.M.'s treating physicians (Drs. Fantasia, Yee, and Bal) in addition to the medical record evidence, were consistent and collectively quite persuasive—along with the testimony of radiologic expert Dr. Silverman. And many of Respondent's arguments focused less persuasively on what the record actually suggested about S.M.'s diagnosis, and more on indirect points about causes that, if established, would at best slightly undermine the TM diagnosis. Such points had some evidentiary heft, but warranted less weight than the record overall.

III. *Petitioners Have Carried Their Burden of Proof Under Althen*

A. Prong One

Petitioners' *Althen* prong one showing was not especially strong, but it was nevertheless sufficient to cross the preponderant "line."

First, I find that both of Petitioners' experts collectively offered enough reliable scientific and medical evidence, bulwarked by their own personal qualifications, to provide a preponderant "can cause" theory relating the Hepatitis B vaccine to TM. They also stated a reasonable immunologic mechanism—molecular mimicry—to explain how the Hepatitis B vaccine can cause TM. First Egan Rep. at 7–8; Second Steinman Rep. at 4–6; Third Steinman Rep. at 2–3. In addition to direct treater support for a causal association (explained in more detail below), Petitioners' experts also propped up their causal theory with references to several case reports, which have *some* probative value in Program cases, even though they do not stand as particularly strong *Althen* prong one evidence. *Doe 93 v. Sec'y of Health & Hum. Servs.*, 98 Fed. Cl. 553, 568 (2011) (citing *Campbell v. Sec'y of Health & Hum. Servs.*, 90 Fed. Cl. 369, 385 (2009)).

Second, existing Program decisions also helped Petitioners somewhat. This is not the first causal opinion in which a petitioner argued that the Hepatitis B vaccine can cause TM in an infant (including those in the mini-omnibus[18] proceedings from approximately sixteen years ago), and I

[18] On October 13-14, 2004, former Special Master (and later Chief Judge of the Court of Federal Claims) Margaret Sweeney held a hearing—which became known as the "Hepatitis B – Neurological Demyelinating Omnibus Proceeding"—to determine whether a causal association exists between the Hepatitis B vaccine and several demyelinating illnesses (multiple sclerosis, TM, chronic inflammatory demyelinating polyneuropathy, and GBS) alleged in four paradigm cases. *Stevens*, 2006 WL 659525; *Werderitsch v. Sec'y of Dept. of Health & Hum. Servs.*, No. 99-638V, 2006 WL 1672884 (Fed. Cl. Spec. Mstr. May 26, 2006); *Peugh v. Sec'y of Dept. of Health & Hum. Servs.,* No. 99–319V, 2007 WL 1531666 (Fed. Cl. Spec. Mstr. May 8, 2007); *Gilbert v. Sec'y of Dept. of Health & Hum. Servs.,* No. 04–455V, 2006 WL 1006612 (Fed. Cl. Spec. Mstr. Mar. 30, 2006). These cases were then reassigned to former Special Master Laura Millman, who found that in all four cases, the Hepatitis B vaccine was causal. *Peugh*, 2007 WL 1006612, at *1, 17–18.

give credence to those prior determinations, which constitute reasoned decisions worthy of my consideration. *See Stevens*, 2006 WL 659525, at *20–25; *Pearson*, 2008 WL 5093378, at *3–4. Such decisions are also distinguishable from those cases involving infants where entitlement was denied, since molecular mimicry is here embraced as the causal mechanism. *See, e.g. Palattao*, 2019 WL 989380, at *33–39. Even though such prior determinations do not mandate the outcome, I reasonably take note of them and their sound rationales.

Petitioners also buoyed their claim with substantial treater support, pointing out the extent to which contemporaneous medical service providers deemed the Hepatitis B vaccine likely causal. *See* Ex. 5 at 18; Tr. at 118–20. Even though much of this evidence bears on the diagnostic question addressed above, or the "did cause" prong, I may also consider it under *Althen* prong one. *Capizzano*, 440 F.3d at 1326 ("[w]e see no reason why evidence used to satisfy one of the *Althen* [ ] prongs cannot overlap to satisfy another prong").The credible testimony of S.M.'s treaters was highly persuasive, and I afford it some weight on the "can cause" element, even if it is less detailed and specific than what Petitioners' causation experts proposed.

Nevertheless, much of the evidence offered by Respondent was similarly persuasive, and it gives me pause in finding for Petitioner. In particular, Respondent's experts have cited a number of persuasive epidemiological studies that undercut the causal theory in this case. *See, e.g.*, Baxter at 1461; Hocine at 5942–43; Schattner at 3877–78. Notably, of these epidemiological studies, Hocine (2007) and Baxter (2016) post-date the omnibus proceedings, including *Stevens* (2006), and Baxter post-dates *Pearson* (2008).[19] Although it is unquestionably the case that Program litigants need not *offer* epidemiological evidence to prevail, special masters may take notes of its existence and consider it when determining if a claimant has met his burden of proof. *See, e.g.*, *D'Toile v. Sec'y of Health & Hum. Servs.*, 726 F. App'x 809, 811–12 (Fed. Cir. 2012). Such evidence does undercut Petitioners' showing—and arguments that I should give case studies great weight, while disregarding large-scale evaluations of vaccination outcomes due to the rarity of vaccine injuries generally, are simply not persuasive.

Petitioners' claim was also weakened—albeit by a smaller degree—by Bogdanos, which Petitioners themselves submitted. As Respondent correctly noted, the amino acid sequence initially identified by Dr. Steinman as the source of homology between components of the Hepatitis B vaccine and MBP is not actually present in Hepatitis B vaccines. Second Kedl Rep. at 4–5. And Dr. Kedl provided credible evidence that the homology between the amino acid sequence later identified by Dr. Steinman in supplemental reports is insufficient to generate cross-reactivity. Second Kedl Rep. at 5–7 (citing Bogdanos at 219; Silvanovich at 252). Indeed, and as I have ruled in other cases, simply proving sequential homology between amino acid sequences in a vaccine component and some self-structure does not automatically make an autoimmune cross reaction

[19] In a recent decision, I gave some weight to the fact that many older decisions involving vaccination and TM did not have the benefit of review of this more-recent epidemiologic evidence. *I.J. v. Sec'y of Health & Hum. Servs.*, No. 16-864, 2021 WL --- (Fed. Cl. Spec. Mstr. Jan. 4, 2021), *appeal docketed* Feb. 3, 2021.

more likely. *See, e.g.*, *Pek v. Sec'y of Health & Hum. Servs.*, No. 16-736V, 2020 WL 1062959, at *16 (Fed. Cl. Spec. Mstr. Jan. 31, 2020).

Overall, after weighing all such evidence in the relevant context, I find that Petitioners have *barely* met their preponderant burden on this first element. Indeed—the evidence is almost in equipoise. But well-reasoned and controlling precedent in the Vaccine Program requires me in such close cases to decide the matter for the petitioner. *See Walther v. Sec'y of Health & Hum. Servs.*, 485 F.3d, 1146, 1150 (Fed. Cir. 2007) ("[u]nder our case law, 'close calls regarding causation are resolved in favor of injured claimants'") (quoting *Althen*, 418 F.3d at 1280)). It is hardly settled in the Vaccine Program that the Hepatitis B vaccine *can* cause TM in children or adults, and a stronger expert showing by Respondent in a future case may tilt the determination in the other direction—especially if coupled with additional evidence. But in this case, I find the "can cause" prong has been satisfied.

B. Prong Two

The record also supports the conclusion that the Hepatitis B vaccine likely caused S.M.'s TM. As previously mentioned, Petitioners offered persuasive testimony from S.M.'s treating physicians—many of whom right away considered a possible association between the Hepatitis B vaccine S.M. received and her subsequent development of TM. While Respondent correctly observes that the record also includes some more ambiguous statements about an association, or may simply have over-relied on the temporal association (which is recognized in the Vaccine Program as an insufficient basis to ascertain causation), I nevertheless discern sufficient, reliable treater support connecting the third dose of the Hepatitis B vaccine S.M. received to her onset of TM shortly thereafter to deem it evidentiarily sufficient.

Petitioners' showing on the "did cause" prong was further bulwarked by the full and extensive effort by S.M.'s treating physicians and Respondent's experts to identify other possible explanations for S.M.'s condition. Bal Rep. at 2–3. While petitioners may not establish entitlement to compensation simply by eliminating other potential causes, this case presents a work-up that was comprehensive. *See* Bal Rep. at 1–3. Petitioners also persuasively established that S.M. was most likely infected with the rhinovirus *during* her hospital admission, diminishing the likelihood that her pre-vaccination sickness was associated with her onset. *Id.* at 2. And the medical record did not establish a likely alternative explanation (although I acknowledge that this record does contain hints of *possible* alternative explanations that Respondent did not fully flesh out).[20]

[20] Had Respondent more directly attempted to preponderantly establish an alternative cause, I would not on this record be able to find that burden was met. *See Deshler v. Sec'y of Health & Hum. Servs.*, No. 16-1070V, 2020 WL 4593162, at *22 (Fed. Cl. Spec. Mstr. July 1, 2020) (citing *de Bazen v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1354 (Fed. Cir. 2008)).

C. Prong Three

Lastly, I find that record evidence in this matter supports the conclusion that the onset of S.M.'s condition occurred within a medically reasonable timeframe, consistent with Petitioners' theory. As noted above, Petitioners assert that S.M.'s symptoms began approximately seventy-seven hours after her receipt of the third Hepatitis B vaccine—a timeframe which has consistently been deemed medically appropriate in *other* cases involving demyelinating conditions, including TM, following vaccination. *See, e.g.*, *Raymo v. Sec'y of Health & Hum. Servs.*, No. 11-654V, 2014 WL 1092274, at *23 (Fed. Cl. Spec. Mstr. Feb. 24, 2014) (onset of TM three to four days after receipt of the Tdap vaccine). Petitioners' experts also credibly explained why a facially-short timeframe for a pathologic process driven by the adaptive immune system, as here, could occur in an infant who had received two prior doses of the same vaccine, and thus whose adaptive response would be inherently faster. First Steinman Rep. at 4.

In reaction, Respondent offered some persuasive evidence to suggest that the onset of S.M.'s condition nevertheless occurred too quickly following immunization to be attributable to an autoimmune process involving the adaptive production of autoantibodies. *See* First Kedl Rep. at 5; Third Kedl Rep. at 5. Dr. Kedl also credibly highlighted that the CSF studies which were performed within hours of S.M.'s symptoms onset were inconsistent with T cell infiltration or cellular damage, as would have been expected under Petitioners' proposed theory. First Kedl Rep. at 5 (citing Ex. 4 at 64).

Dr. Kedl's opinion was certainly reliable and well-founded, and as such, it merited careful consideration. But in weighing this evidence against that offered by Petitioner and prior Program cases, I find it merely (again) brought the parties closer to equipoise—supporting a determination in Petitioners' favor.

CONCLUSION

This matter serves as a case study for how the preponderant evidentiary standard often functions in practice. Putting aside the parties' dispute over the precise nature of S.M.'s injury (a matter that was easily decided in Petitioners' favor), it has not been established to any degree of scientific certainty that the Hepatitis B vaccine can cause TM—especially in the fairly short timeframe at issue here. Many of the arguments mustered by Petitioners' experts invoke causation contentions that either hold less and less weight as science progresses (especially in light of recent epidemiologic studies), or reflect standard points experts nearly always assert in Program cases (such as recitation of the magic words "molecular mimicry") but which do not equally carry the same weight in all cases.

But scientific certainty is *far* from the evidentiary standard to be applied in Program cases. Indeed, Vaccine Program claimants can prevail *despite* the fact that considerable uncertainty remains that they are correct. "More likely than not" is an inexact measurement to say the least.

Thus, I must conclude on the basis of Petitioners' showing *in this case* that they have met their evidentiary burden. The mix of treater support specific to S.M., plus on-point prior decisions regarding the Hepatitis B vaccine and TM, are particularly compelling evidence, along with other reliable science generally supporting Petitioners' contentions. Under such circumstances, a favorable award is legally appropriate, and consistent with the generous policy goals of the Program. The Act expressly seeks to compensate parties like the McGrails who have needlessly suffered, as so amply demonstrated by the facts of this case, and thus the evidence adduced herein supports a favorable entitlement decision.

In order to guide the parties through the damages phase of the action, a separate damages order will issue.

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Chief Special Master